Effects of increasing flow rate on aortic stenotic indices: evidence from percutaneous transvenous balloon dilatation of the mitral valve in patients with combined aortic and mitral stenosis

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Abstract

Objectives—To investigate the effects of transvalvar flow rate on aortic valve resistance and valve area after percutaneous transvenous balloon dilatation of the mitral valve in a homogeneous group of patients with rheumatic heart disease.

Design—Retrospective analysis of 12 patients with combined aortic and mitral stenosis who had undergone balloon dilatation of the mitral valve over a period of 9 years.

Setting—Tertiary referral centre.

Patients—Twelve (8 women, 4 men; mean (SD) age 37 (9)) of 227 consecutive patients with critical mitral stenosis undergoing transvenous balloon dilatation of the mitral valve in the centre also had aortic stenosis, defined as a transaortic pressure gradient of more than 25 mm Hg measured at a catheterisation study before valvuloplasty.

Interventions—Echocardiographic variables (mitral valve area measured by the pressure half-time method and planimetry, and the aortic valve area derived from the continuity equation) and haemodynamic measurements (cardiac output, left ventricular mean systolic pressure, aortic mean pressure, transaortic valve pressure gradient, mitral valve and aortic valve areas derived from the Gorlin formula, and aortic valve resistance) were assessed before and after transvenous balloon dilatation of the mitral valve. Follow up catheterisation to measure haemodynamic variables was performed one week after mitral valvuloplasty.

Results—Mean transaortic flow rate increased 33% after mitral valvuloplasty (from 198 (68) to 254 (41) ml/s, P = 0·002). Aortic valve areas derived from the Gorlin formula were significantly increased from 0·57 (0·12) to 0·73 (0·14) cm² (P = 0·006) after mitral valvuloplasty. However, aortic valve area and valve resistance derived from the continuity equation were independent of the increase in flow rate after mitral valvuloplasty (from 1·29 (0·35) to 1·30 (0·29) cm² and from 317 (65) to 259 (75) dyn·s·cm⁻⁵, both P = NS).

Conclusion—The Gorlin-derived aortic valve area tends to be flow-dependent, and continuity equation-derived aortic valve area and catheterisation-derived valve resistance seem to be less flow-dependent. In patients with combined mitral and aortic stenosis, these flow-independent indices are important for decision-making.

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Various methods can be used to determine aortic valve area. However, haemodynamic determination of valve area by the Gorlin formula[1] is often used to gauge the severity of aortic valve stenosis.[2] The accuracy of this formula for assessment of aortic valve area has been challenged.[3 4] Several groups have indicated that the calculated valve area varies directly with cardiac output,[5–8] and that an increased transvalvar flow rate will increase the calculated valve area. The dependence of calculated valve area on transvalvar flow rates seems to be particularly important when flow rates are low; this may result in overestimation of the severity of aortic stenosis, especially in patients with combined mitral stenosis.

Aortic valve area derived from the Doppler continuity equation and haemodynamically derived valve resistance are viewed as indices of the severity of aortic stenosis that are less flow-dependent. The Gorlin equation measures anatomical valve area by assuming that it maintains a constant ratio with the flow-dependent coefficient of orifice contraction. However, the continuity equation measures the effective orifice area (the area of the vena contracta) without making any assumptions. Haemodynamically derived valve resistance (the simple ratio of mean transvalvar pressure difference to mean flow rate) was proposed as an index of stenosis many years ago.[9–11] Studies have shown that when the pressure gradient was varied the Gorlin-calculated valve area changed at least three times more than resistance. Valve resistance seems to be less flow-dependent.[12 13] However, in dogs Burwash *et al*[6 7] showed a degree of flow-dependence of the aortic valve area derived from the continuity equation and of valve resistance that was similar to the Gorlin-derived aortic valve area.

We have investigated the effect of increasing transvalvar flow rate on aortic valve areas derived from the Gorlin and Doppler echocardiography continuity equations and on haemodynamically measured valve resistance.

Patients and methods

PATIENTS

Between July 1987 and May 1995, 227 patients with symptomatic mitral stenosis underwent balloon dilatation of the mitral valve at the National Taiwan University Hospital. Twenty one patients had concomitant transaortic mean pressure gradients ⩾ 25 mm Hg measured during the prevalvuloplasty catheterisation study. Surgical valve replacement was suggested for all these patients. The 12 patients who were reluctant to undergo valve replacement became the study group. All patients signed informed consent sheets for balloon dilatation of the mitral valve. The eight women and four men were aged 37 (9) (SD) (range 20–61).

ECHOCARDIOGRAPHIC ASSESSMENT

Study patients had cross sectional echocardiography with Doppler colour flow mapping one to two days before and one to three days after balloon dilatation of the mitral valve. A Hewlett-Packward Sonos 1000 or 1500 was used. The severity of mitral regurgitaiton and aortic regurgitation was assessed as described by Abascal *et al*[14] and Otto *et al*.[15] Mitral valve area was calculated by the Doppler pressure half-time method[16] and planimetry. In the planimetry method the smallest orifice of the mitral valve was identified in the parasternal short axis view and the valve area was measured at maximum opening in diastole on a freeze-frame image. None of the patients had an echocardiographic valve score of > 8 on a scale of 16.[15] Aortic valve area was calculated by continuity equation[14] as follows:

$$Ac = A_{LVOT} \cdot V_{LVOT}/V_{max}$$

where, Ac = aortic valve area, A_{LVOT} = the cross sectional area of the left ventricular outflow tract, V_{LVOT} = flow velocity in the left ventricular outflow tract before the aortic valve, obtained by the pulsed Doppler method, and V_{max} = the highest maximal poststenotic jet velocity, recorded by continuous wave Doppler from the apical view. Measurements in patients with atrial fibrillation were averaged for five consecutive beats. Video images were recorded for off-line analysis.

CATHETERISATION

Before balloon valvuloplasty, diagnostic right and left catheterisation was performed from a femoral approach. Baseline heart rate, cardiac output, and left ventricular and systemic arterial pressure were measured. Cardiac output was determined by the thermodilution method in triplicate or quadruplicate by injecting 10 ml of ice-cold saline solution. Left ventricular and femoral artery pressures were measured with simultaneous recordings by a catheter and sidearm sheath. To spare patients the added discomfort and risk of a second aortic catheterisation, femoral artery pressure was used instead of pressure in the ascending aorta.[17] Simultaneously measured left ventricular-femoral artery gradients represented transaortic pressure gradients. After baseline prevalvuloplasty haemodynamic measurements were obtained, transseptal puncture was performed. Balloon mitral valvuloplasty was performed with an Inoue balloon catheter (26–28 mm). Sequential inflations were performed at increasing diameters until a balloon waist disappeared. After balloon mitral valvuloplasty, right and left heart catheterisation was repeated by the same cardiac catheterisation procedure. The shunt ratio of the atrial septal defect was calculated from the oxygen saturation differences. Valve areas were calculated using the Gorlin formula[1]:

Aortic valve area (cm²) = $CO/44\cdot3\cdot HR\cdot SEP\cdot$(transaortic mean pressure gradient)$^{1/2}$ where CO is cardiac output (ml/min), HR is heart rate (beats/min), and SEP is systolic ejection period (seconds/beat).

Mitral valve area (cm²) = $CO/38\cdot HR\cdot DEP\cdot$(transmitral mean pressure gradient)$^{1/2}$ where CO is cardiac output (ml/min), HR is heart rate (beats/min), and DEP is diastolic ejection period (seconds/beat).

Aortic valve resistance (dyn·s·cm⁻⁵) = $1333\cdot$mean $PG\cdot HR\cdot SEP/CO$ where PG is transaortic pressure gradient (mm Hg), HR is heart rate (beats/min), SEP is systolic ejection period (seconds/beat), and CO is cardiac output (ml/min). Follow up catheterisation was performed for haemodynamic measurements and cardiac output one week after the first catheterisation.

STATISTICAL ANALYSIS

Values are expressed as mean (SD). Changes in echocardiographic and haemodynamic variables were evaluated with paired *t* test. Catheterisation and Doppler measures of the severity of aortic stenosis were compared by linear regression. A probability (P) value of less than 0·05 was regarded as significant.

Results

EFFECT OF CHANGING FLOW RATE ON AORTIC VALVE AREA AND VALVE RESISTANCE

Transthoracic echocardiographic and haemodynamic variables before and after balloon mitral valvuloplasty are shown in table 1. Mean transaortic pressure gradient before valvuloplasty was 34 (7) mm Hg. Mitral valve areas measured by planimetry, the Doppler

Table 1   Measurements (mean (SD)) before and after balloon dilatation of the mitral valve in the 12 study patients

Variables	Before PTMV	After PTMV	P value
HR (min⁻¹)	72 (8)	73 (6)	NS
CO (l/min)	3·6 (0·1)	4·2 (0·5)	0·01
CI (l/min·m²)	2·2 (0·3)	2·6 (0·3)	0·01
Flow rate (ml/s)	198 (68)	254 (41)	0·002
Transaortic mean pressure gradient (mm Hg)	34 (7)	37 (13)	0·006
Diastolic ejection time (s/beats)	0·473 (0·042)	0·438 (0·062)	NS
Systolic ejection time (s/beats)	0·345 (0·035)	0·308 (0·045)	0·03
Mitral valve area (cm²):			
Doppler t1/2	0·86 (0·17)	1·63 (0·22)	< 0·0001
Planimetry	0·78 (0·18)	1·73 (0·21)	< 0·0001
Gorlin formula	0·83 (0·12)	1·48 (0·26)	< 0·0001
Aortic valve area (cm²):			
Continuity equation	1·29 (0·35)	1·30 (0·29)	NS
Gorlin formula	0·57 (0·12)	0·73 (0·14)	0·006
Aortic valve resistance (dyn·s·cm⁻⁵)	317 (65)	259 (75)	NS

CI, cardiac index; CO, cardiac output; PTMV, percutaneous transvenous mitral valvuloplasty.

pressure half-time method, and Gorlin formula were significantly increased from 0·78 (0·18) to 1·73 (0·21) cm², from 0·86 (0·17) to 1·63 (0·22) cm², and from 0·83 (0·12) to 1·48 (0·26) cm², respectively (all P < 0·0001). In response to mitral valvuloplasty, cardiac output and cardiac index significantly increased from 3·6 (0·1) to 4·2 (0·5) l/min and from 2·2 (0·3) to 2·6 (0·3) l/min per m² (both P = 0·01), predominantly because of the increase in stroke volume instead of heart rate. The systolic ejection time was significantly decreased after mitral valvuloplasty. Mean transaortic flow rate increased 33% from 198 (68) to 254 (41) ml/s (P = 0·002). The flow rate at follow up catheterisation (265 (46) cm/s) did not show significant change compared with that immediately after balloon mitral valvuloplasty. The Gorlin-derived aortic valve area ranged from 0·42 to 0·85 cm² with a mean of 0·57 (0·12) cm² before mitral valvuloplasty, and increased to a mean of 0·73 (0·14) cm² after mitral valvuloplasty (P = 0·006). The aortic valve area derived from the continuity equation remained steady at 1·29 (0·35) and 1·30 (0·29) cm² respectively. The correlation coefficient for Gorlin-derived and continuity equation-derived aortic valve areas was 0·57 (Gorlin valve area = 0·185·continuity equation valve area + 0·334, SEE = 0·099 cm²) before valvuloplasty. However, the correlation coefficient was 0·75 after valvuloplasty (Gorlin valve area = 0·351·continuity equation valve area + 0·276, SEE = 0·097 cm²). Aortic valve resistance was not significantly changed after valvuloplasty (317 (65) *v* 259 (75) dyn·s·cm⁻⁵, P = NS).

Discussion

EFFECTS OF FLOW RATE ON STENOTIC INDICES
In this study aortic valve area derived from the Doppler echocardiographic continuity equation and haemodynamically derived valve resistance were less flow dependent than the Gorlin-derived aortic valve area. Several previous studies consistently found that Gorlin valve areas changed with volume flow rate both in vitro[18] and in patients.[19 20] Gorlin valve areas increased 19% to 50% when transvalvar volume flow rate increased by 50%. In the current study there was a 33% increase of transaortic flow rate and a 27% increase in Gorlin-derived aortic valve area after balloon mitral valvuloplasty. The change in Gorlin-derived valve areas may partly be the result of a "true" change in anatomical area. Video

images of in vitro pulsatile flow models have shown that the valve orifice does increase with increasing volume flow rate,[21 22] presumably because greater flow-mediated force is delivered to the non-rigid valve. However, changes in Gorlin-derived valve areas caused by changes in volume flow rate in patients here can not be totally explained by anatomical flow-dependent changes because rheumatic aortic valves have fixed valves even at the early stage of rheumatic heart disease. Discharge coefficients in the Gorlin constant were assumed to be fixed which may not accurately reflect stenotic valve geometry.[4] Indeed, the discharge coefficients have never been validated in native aortic valve stenosis.

Previous studies of the flow dependence of the continuity equation-derived valve area and haemodynamically derived valve resistance had inconsistent results (table 2).[5 6 8] Several studies showed constant continuity equation-derived valve areas and valve resistance despite an increase in volume flow rate, as we did in the present study. However, the continuity equation-derived valve areas were shown to be flow-dependent in an in vitro study[21] and in patients.[6 23] There may be an explanation for these discordant observations. First, the aortic stenosis studied was of different severity and cause. Table 2 shows that Cannon *et al*[5] reported that a heterogeneous group of patients with severe aortic stenosis and clinical symptoms had constant continuity-equation valve areas and valve resistance with increases in volume flow rate. When severe aortic stenosis develops, especially that associated with degeneration, aortic valves become immobile, heavily calcified, and non-flexible. Immobile aortic valves are not likely to respond to flow rate changes. Thus orifice areas would not be expected to change when volume flow rate increases in patients with severe aortic stenosis. Patients with severe and immobile aortic valves will have constant continuity equation valve areas. In this study, because the patients were relatively young and had mild aortic stenosis, their aortic valves were probably more flexible. However, this is the first study of indices of aortic valve stenosisc during flow rate changes in a homogeneous group of rheumatic heart disease patients. Compared with degenerative aortic stenosis, rheumatic aortic stenosis is characterised by a tricuspid valve with fusion of one to three commissures and densely fibrotic cusps resulting in fixed aortic valves during the early stage of rheumatic heart disease. Findings showed

Table 2   Discordant results of flow-independence of aortic valve area and valve resistance

Study	No	Symptoms	Method	Intervention	CO (l/min)	Flow rate (ml/s)	PG (mm Hg)	Flow dependent	Flow independent
Cannon *et al*[5]*	4	Yes	Cath	Nitroprusside	50%	—	−7%	G-AVA	Valve resistance
Burwash *et al*[6]	66	No	Echo	Exercise	—	24%	36%	C-AVA, Valve resistance	
Casale *et al*[8]	12	—	Cath	Dobutamine	38%	34%	25%	G-AVA	C-AVA, Valve resistance
This study	12	Yes	Cath	PTMV	19%	33%	9%	G-AVA	C-AVA, Valve resistance

*The values were calculated from mean values of cardiac output and pressure gradient. —, no data available; C-AVA, aortic valve area derived from the continuity equation; cath, catheterisation; CO, cardiac output; echo, echocardiography; G-AVA, Gorlin-derived aortic valve area; PG, pressure gradient; PTMV, percutaneous transvenous mitral valvuloplasty.

constant continuity equation valve areas similar to those in patients with severe aortic stenosis. Burwash et al[67] studied patients with non-critical aortic stenosis without symptoms who had more flexible valves,which explains why their continuity equation valve areas were flow-dependent. These observations support the hypothesis that the severity and cause of aortic stenosis are important in the interpretation of severity indices. Second, the discrepancy may relate in part to methodological differences. Burwash et al[67] demonstrated the flow dependence of valve resistance calculated from Doppler echocardiography instead of from conventional invasive catheterisation. The inherent limitations of echocardiography in measuring simultaneous transvalvar and left ventricular outflow tract velocities and sampling sites before pressure recovery may have confounding effects on conclusions.

POTENTIAL LIMITATIONS
There were several potential limitations in this study. First, atrial fibrillation was present in nine of the 12 subjects. This would be expected to affect the accuracy of valve area (Gorlin and continuity equation) and valve resistance. It became difficult to obtain the simultaneous pressure gradients and flow measurements required for accurate invasive measurement of indices of stenosis. Second, in this study all patients had variable degrees of mild to moderate aortic regurgitation of a rheumatic nature which would cause underestimation of cardiac output by the thermodilution method. The Gorlin method overestimates the severity of stenosis in false low cardiac output states. This may in part explain the great differences between aortic valve areas derived from the Gorlin and continuity equations. Third, the Gorlin aortic valve area and continuity equation valve area were not derived simultaneously. Though transvalvar flow had changed between the times of the two Gorlin aortic valve area measurements, we do not know whether transvalvar flow rate was different at the time of the two continuity equation valve area measurements. However, the flow rates at follow up catheterisation one week after balloon mitral valvuloplasty were not significantly different compared with those measured immediately after balloon mitral valvuloplasty. Thus the difference of measurement timing is unlikely to have affected the results. Fourth, there is no "gold standard" measurement of true anatomical valve area in vivo with which to compare the observed valve area. Thus the real increase of anatomical valve area or its reflection in flow dynamics can not be determined. Fifth, the study group is small; nevertheless, it does suggest a new approach to stenotic indices after balloon mitral valvuloplasty. These findings need to be be confirmed in a larger study.

CLINICAL IMPLICATIONS
The flow-dependence of the Gorlin aortic valve area may significantly influence clinical decision-making. A critical aortic area calculated by Gorlin formula may not be a "true"

critical lesion, especially when flow is low as it is when aortic stenosis is combined with mitral stenosis. Before patients with combined aortic and mitral stenosis are subjected to double valve replacement or valvuloplasty, aortic valve areas derived from the continuity equation and haemodynamially derived valve resistance (which are less flow-dependent) should be measured to reflect the true severity of aortic stenosis.

CONCLUSIONS
In patients with combined aortic and mitral stenosis who have low cardiac output, the Gorlin-derived aortic valve area tends to overestimate the severity of aortic stenosis.The aortic valve area derived from the Doppler echo continuity equation and haemodynamically derived valve resistance seem less flow-dependent and more useful clinically, especially in patients with immobile valves.

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